7. The method of claim 1, wherein the portion of biglycan [is] comprises at least one [or more 24 amino acids] repeat motif[s] of 24 amino acids in the Leucine Rich Repeat (LRR) of [human biglycan having] SEQ ID NO: 9.

8. The method of claim 7, wherein the biglycan comprises an amino acid sequence comprising one or more [LLRs] LRRs of [human biglycan having] SEQ ID NO: 9.

11. The method of claim 10, wherein the biglycan comprises an amino acid sequence that is at least about 95% identical to amino acids 38-365 of SEQ ID NO: 9.

12. The method of claim 1, wherein the biglycan is encoded by a nucleic acid which hybridizes under stringent conditions of 6.0 x sodium chloride/sodium citrate (SSC) at about 45 °C to SEQ ID NO: 8.

13. The method of claim 1, wherein the biglycan [is Torpedo DAG-125 comprising] comprises the amino acid sequences of SEQ ID NOs: 1-3.

REMARKS

Upon entry of this amendment, claims 1-14 constitute the pending claims in the present application. Claims 15-52 are withdrawn from consideration as being drawn to a non-elected invention. Applicants will cancel these claims upon indication of allowable subject matter in the elected invention. Claims 1-2, 4, 7-8, and 11-12 have been amended. Applicants submit that no new matter has been introduced by the amendments to these claims, and that the amendments are fully supported by Applicants' original specification and claims. The amendments are made solely to expedite prosecution of the application, and Applicants reserve the right to prosecute claims of similar or differing scope in subsequent applications.

Applicants note that the Examiner has acknowledged Applicants' election of Group I with traverse in the reply dated 7/1/2002 (Paper No. 16). Applicants also note

that the Examiner has renumbered the original mis-numbered claims 1-4, 16-28, and 30-54 to claims 1-52.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Oath/Declaration

The Office Action points out that the oath or declaration is defective. Applicants enclose herewith a supplemental application data sheet which identifies the post office address of inventor J. R. Fallon (see 37 CFR 1.76(c)). Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Claim rejections under 35 U.S.C. 112, first paragraph

Claims 1-6 and 9-14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Particularly, the Office Action asserts that these claims are directed to methods employing biglycan or a protein having an amino acid sequence with 90% identity to a portion of biglycan, or 95% identity to amino acids 38-365 of SEQ ID NO: 9. However, the specification allegedly fails to describe a complete structure of the entire genus of proteins encompassed by these claims. The Office Action further alleges that the claims fail to recite other relevant identifying characteristics (physical, chemical, and/or functional characteristics coupled with a known or disclosed correlation between function and structure).

Although Applicants believe that the application as filed provides adequate description of various biglycan structures, in order to expedite prosecution, Applicants have amended independent claim 1 to clarify that biglycan polypeptides encoded by the claimed genus of polypeptides comprise a sequence at least 80% identical to SEQ ID NO: 9 or a portion thereof, and possess DAPC-stabilizing activity. As amended, claim 1 and

dependent claims 2-14 recite identifying physical and/or chemical characteristics (i.e., being at least 80% identical to SEQ ID NO: 9, or a portion thereof) and functional characteristics (i.e., possessing DAPC-stabilizing activity). Similarly, Applicants have amended claim 2 to specify the biglycan polypeptide by using a SEQ ID NO. Accordingly, Applicants submit that the correlation between structure and function requested by the Examiner is now present in the claimed genus, and no structurally or functionally unrelated polypeptides fall within the scope of the amended claims.

Since the test of enablement is whether "any person skilled in the art can make and use the invention without undue experimentation (*In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988)" (MPEP 2164.01), Applicants submit that the amended claims are enabled to the full claimed scope. Therefore, reconsideration and withdrawal of the rejection under 35 U.S.C. 112, first paragraph, is respectfully requested.

Claim rejections under 35 U.S.C. 112, second paragraph

Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Specifically, the Office Action asserts that claims 1-6, 9, and 12-14 are vague and indefinite due to the use of the term "biglycan" as a limitation. As described above, Applicants believe that the term "biglycan" is not indefinite. Nonetheless, in order to expedite prosection, independent claim 1 has been amended to define "biglycan" as comprising a sequence at least 80% identical to SEQ ID NO: 9 or portions thereof, and possessing DAPC-stabilizing activity. Accordingly, a skilled artisan would readily understand the metes and bounds of the term "biglycan" in these claims. Therefore, reconsideration and withdrawal of the rejection is respectfully requested.

The Office Action points out that claims 3-6 refer to the limitation "biglycan" in claim 2, but claim 2 recites "biglycan" three times, making it unclear which "biglycan" is being referred to. As described above, Applicants have amended claim 2, rendering this ground of rejection moot.

The Office Action points out that claim 7 recites the limitation "portion of biglycan" in claim 1. However, there is insufficient antecedent basis for this limitation in the claim. As described above, Applicants have amended claim 1 by including "a portion," thereby rendering this rejection moot.

The Office Action points out that claim 8 recites the limitation "biglycan" and the limitation "LLR" in claim 7. However, there is insufficient antecedent basis for this limitation in the claim. To overcome this rejection, Applicants have amended claims 7 and 8. As amended, claim 7 recites "biglycan" only once, and the typographic error "LLR" in claim 8 is changed to "LRR."

The Office Action asserts that claim 13 is vague and ambiguous for recitation of "Torpedo DAG-125" biglycan. The Examiner argues that without precise molecular sequence supported by a proper sequence identifier, the metes and bounds of "Torpedo DAG-125" biglycan cannot be determined. Solely to expedite prosecution of the application, Applicants have amended claim 13 to replace the "Torpedo DAG-125" with the biglycan that "comprises the amino acid sequences of SEQ ID NOs: 1-3."

The Office Action asserts that claims 10 and 11 are indefinite for being dependent from the indefinite claim (i.e., claim 1). As described above, Applicants have amended claim 1, rendering this rejection moot.

Based on the above arguments, Applicants submit that all claims as amended comply with the requirement of 35 U.S.C. 112, second paragraph. Therefore, reconsideration and withdrawal of rejections under 35 U.S.C. 112, second paragraph, is respectfully requested.

Claim rejections under 35 U.S.C. 102

Claims 1-6, 9, and 12 are rejected under 35 U.S.C. 102(b), as being anticipated by Ruoslahti et al. (WO 93/10808, 1993). The Ruoslahti reference allegedly describes a method for treating a pathology characterized by an accumulation of extracellular matrix in a tissue by contacting said tissue with an agent that suppresses the extracellular matrix producing activity of TGF-β, wherein said agent is biglycan. The Office Action further

alleges that by contacting the tissue with biglycan, stabilization of dystrophin-associated protein complexes (DAPCs) is achieved, absent evidence to the contrary. Applicants respectfully disagree for the reasons that follow.

To anticipate an invention, the prior art reference must disclose each and every aspect of the claimed invention. Thus, to anticipate the method of amended claims 1-14, a prior art reference would have to disclose a method for stabilizing dystrophin-associated protein complexes (DAPCs) on the surface of a cell, comprising contacting the cell with an effective amount of biglycan, such that the DAPCs are stabilized, wherein said biglycan comprises a sequence at least 80% identical to SEQ ID NO: 9 or a portion thereof, and possesses DAPC-stabilizing activity.

Ruoslahti et al. do not describe any biglycan in particular, and do not specify a biglycan comprising a sequence at least 80% identical to SEQ ID NO: 9 or a portion thereof, and possesses DAPC-stabilizing activity.

Dependent claims 3-6, 9, and 12 are not anticipated by the Ruoslahti reference for the same reasons described as above.

Claims 3-6 are allegedly anticipated by Ruoslahti et al. because the Examiner asserts that the biglycan used in the method disclosed by Ruoslahti et al. inherently holds the same properties (i.e., being able to bind to alpha-dystroglycan, alpha-sarcoglycan and/or gamma-sarcoglycan, and also stimulate phosphorylation of alpha-sarcoglycan on a cell membrane) as the biglycan used in the instant invention, absent evidence to the contrary. Applicants respectfully submit that this dependent claim is free of the art for the same reasons provided with respect to the corresponding independent claims.

Claim 9 is allegedly anticipated by Ruoslahti et al. because the Examiner asserts that the biglycan of the Ruoslahti reference may comprise glycosaminoglycan (GAG) side chains as well. Applicants respectfully submit that this dependent claim is free of the art for the same reasons provided with respect to the corresponding independent claims. Thus, in the absence of teachings of the biglycan structures in the Ruoslahti reference, a skilled artisan would not necessarily expect that the biglycan comprises GAG side chains.

Claim 12 is rejected because of the recitation of "encoded by a nucleic acid which hybridizes to SEQ ID NO: 8." Applicants submit that claim 12 depends from claim1 and the biglycan in claim 12 is thereby limited to comprising a sequence at least 80% identical to SEQ ID NO: 9 or a portion thereof, and possessing DAPC-stabilizing activity. Nevertheless, solely to expedite prosecution of the application, Applicants have amended claim 12 to specify the stringent hybridization condition as "of 6.0 x sodium chloride/sodium citrate (SSC) at about 45 °C." Support for such amendment can be found in the specification, e.g., page 23, lines 20-23. As amended, the method of claim 12 does not encompass use of any biglycan molecule regardless of its structure, since the biglycan is clearly defined.

Based on the above arguments, Applicants submit that the cited Ruoslahti reference fails to anticipate amended claims 1-14. Therefore, reconsideration and withdrawal of the rejection under 35 U.S.C. 102 is respectfully requested.

Claim rejections under 35 U.S.C. 103(a)

Claims 7-8, 10-11, and 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ruoslahti et al.

Specifically, the Office Action asserts that Ruoslahti et al. neither expressly disclose particular biglycans nor provide a specific amino acid or encoding sequences for identification of biglycans used in the disclosed method. However, the Office Action asserts that at the time of invention was made, it would have been *prima facie* obvious to a person of ordinary skill in the art to employ human biglycan in a method disclosed by Ruoslahti et al.. The Office Action further alleges that one of ordinary skill in the art would have been motivated to do this because the disclosure of Ruoslahti et al. encompasses the use of biglycan without adding any limitation to its structure, source, method of purification or synthesis or derivation from a specific species. Applicants respectfully traverse this rejection to the extent it is maintained over the claims as amended.

Pursuant to MPEP 2143, "[t]o establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in

the reference themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations."

As discussed above, Ruoslahti et al. do not teach or suggest the selection of a biglycan that comprises a sequence at least 80% identical to SEQ ID NO: 9 or a portion thereof, and possesses DAPC-stabilizing activity. Ruoslahti et al. fail to provide any structural or functional characteristics of the biglycan to be used. The Examiner has cited no art linking suppression of extracellular matrix production to DAPC stabilization. Accordingly, the Examiner has failed to cite reference teaching or suggesting the methods of claim 1 and claims depending therefrom.

In addition, a skilled artisan would not have had a reasonable expectation of success even if, for the sake of argument, the Ruoslahti reference were combined with specific biglycan sequences. Ruoslahti et al. at most suggest that the biglycan suppresses the extracellular matrix producing activity of TGF-β and is used for reducing accumulation of extracellular matrix. Absent a teaching that the two functions are somehow related, one of skill in the art could not predict that a biglycan that possesses one of these functions would also possess the other. Therefore, even based on the combination of the Ruoslahti reference and specific biglycan sequences, a skilled artisan still would not have had a reasonable expectation of success to use a biglycan to stabilize DAPCs on the surface of a cell.

Accordingly, Applicants submit that at least two of the three requirements for establishing a *prima facie* case of obviousness are missing. Reconsideration and withdrawal of rejection under 35 U.S.C. 103(a) is respectfully requested.

CONCLUSION

For the foregoing reasons, Applicants respectfully request reconsideration and withdrawal of the pending rejections. Applicants believe that the claims are now in

condition for allowance and early notification to this effect is earnestly solicited. Any questions arising from this submission may be directed to the undersigned at (617) 951-7000.

If there are any other fees due in connection with the filing of this submission, please charge the fees to our **Deposit Account No. 18-1945.** If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit account.

Respectfully Submitted,

Date: December 11, 2002

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